DRAWING AMENDMENTS

The attached sheet of drawings includes changes to Figure 11. This sheet replaces the original sheet including Figure 11. In Figure 11, the previously omitted label along the Y-axis has been added.

REMARKS

OATH OR DECLARATION

Applicants acknowledge the requirement for a new oath or declaration in compliance with 37 CFR 1.67(a). Applicants request that this issue be placed in abatement until allowable subject matter has been indicated.

DRAWINGS

The examiner has objected to Figure 11 for lacking a labelled Y-axis, and to Figure 12 for allegedly showing contradictory results for time optimization of translation reaction. Applicants submit a corrected Figure 11, and correct a typographical error in the specification, thus clarifying Figure 12.

The corrected Figure 11 depicts relative absorbance units along the Y-axis. Figure 11 shows the time course of translation of CAT mRNAs (discussed in Example 5) using the HeLa cell extract (p. 13, lines 23-24) (the preparation of which is described in Example 4). Example 5 states "*Translational efficiency is judged by the amount of the CAT protein (ng) measured by a colorimetric enzyme immunoassay (CAT ELISA, Böhringer Mannheim).*" (p. 20, lines. 23-24). This assay uses a peroxidase-labelled secondary antibody and the peroxidase substrate ABTS. Thus, corrected Figure 11 has a Y-axis in relative absorbance units showing the results of the CAT ELISA of Example 5.

Regarding Figure 12, Applicants have amended the specification to correct a typographical error, thus clarifying the results shown in Figure 12. Applicants have replaced "Figure 8" with "Figure 12" at page 21, line 4. The amended application states: "*Figure 12 shows a northern blot analysis of the transcripts during the translation assay. Bars represent radioactive intensity of each messenger measured by a phosphoimager. Graph (A) shows the*

four messengers at different times, from 0 to 150 minutes. Graph (B) shows the Cap and the Cap-pA transcripts from 0 to 90 min." (page 21, lines 4-7) Figure 12 therefore illustrates 2 sets of experimental results depicting CAT transcript stability over time (and not translation efficiency or time optimization of translation reaction) and shows that "*uncapped mRNA are...rapidly degraded*" (p. 21, lines 11-12). Thus, Figure 12 graphs A and B are not contradictory and Applicants respectfully request that the drawing rejection of Figure 12 be withdrawn.

Applicants also would like to note that, on page 21, line 16, the reference to "Figure 9" is clearly a typographical error; the reference should be to Figure 13. Applicants have amended the specification to correct this error.

SUPPORT FOR NEW CLAIMS AND REASONS FOR AMENDMENTS

Applicants cancel pending claims 1 – 44, and submit new claims 45 – 60 according to the Revised Format of Amendments. These amendments are made to clarify the claims in order to expedite allowance of the present application. Applicants reserve the right to prosecute cancelled claims in this or other applications. The new claims generally conform to the cancelled claims, add no new subject matter, and are fully supported throughout the specification and by the drawings and claims as filed. Support for new claims 45 – 60 can be found throughout the specification, drawings, and claims as filed. In particular, support for new independent claim 45 is found in original independent claim 1.

APPLICANT'S CLAIMED INVENTION IS NOT ANTICIPATED UNDER 35 USC §102(b) IN VIEW OF IIZUKA *ET AL.* (1994)

Applicants' claimed invention is not anticipated by prior art prior to amendment. To expedite allowance of the application, however, Applicants submit this amendment to clarify the claimed invention.

The Examiner alleges that claims 1 – 4 are anticipated under 35 USC §102(b) in view of Iizuka *et al.* (1994). In rejecting claim 1, the examiner cites Iizuka *et al.* as teaching *in vitro* translation of an mRNA with both a 5' cap and a 3' poly-A tail by incubating a cell extract of a multicellular eukaryote (rabbit reticulocytes or wheat germ) with the RNA template under translation conditions such that protein production is greater than the sum of the protein production where the RNA template includes only a 3' cap and the protein production where the RNA template includes only a 5' poly(A) tail. The examiner has also rejected claims 2, 3, and 4, citing Iizuka *et al.* as teaching use of an animal cell extract (referring to claim 2), and a human cell extract (referring to claims 3 and 4). Applicants respectfully disagree with the Examiner's allegations of anticipation for the following reasons.

Iizuku *et al.* do not in fact show that protein production where the RNA template includes both a 3' cap and a 5' poly(A) tail is greater than the sum of the protein production where the RNA template includes only a 3' cap and the protein production where the RNA template includes only a 5' poly(A) tail. This reasoning is based on both the data shown in Iizuku *et al.* as well as the authors' own statement.

The data in Iizuka *et al.* show that, in rabbit reticulocytes, protein production (as measured by relative luciferase activity) where the template has both a 5' cap and a 3' poly-A tail (3.7 relative units) is <u>not</u> greater than the sum of the protein produced where the template has only a 5' cap (2.6 relative units) and the protein produced where the template has only a 3' poly-

A tail (1.5 relative units). Iizuka *et al.* also show that, in human (HeLa) cells, protein production where the template has both a 5' cap and a 3' poly-A tail (1.3 relative units) is not greater than the sum of the protein produced where the template has only a 5' cap (1.3 relative units) and the protein produced where the template has only a 3' poly-A tail (0.97 relative units).

Furthermore, Iizuka *et al.* explicitly state that:

> "However, this cooperation [between a 7mG cap and a poly(A) tail] was **not observed in extracts prepared from human HeLa cells (Fig. 4, lanes 16-20) or rabbit reticulocyte lysates (Fig. 4, lanes 1-5)**, in agreement with observations of *in vivo* translations made by Gallie." (p. 7326, para. 2) [emphasis added]

Thus, Iizuka *et al.* do not teach *in vitro* translation of an mRNA with both a 5' cap and a 3' poly-A tail by incubating a cell extract of an animal with the RNA template under translation conditions such that protein production is greater than the sum of the protein production where the RNA template includes only a 3' cap and the protein production where the RNA template includes only a 5' poly(A) tail.

Accordingly, the claimed invention is not anticipated by Iizuka *et al.*, and Applicants respectfully request that the rejection be withdrawn. To expedite allowance of the application, however, Applicant has cancelled claims 1 – 44, and provided new claims 45 – 60.

APPLICANT'S CLAIMED INVENTION IS NOT OBVIOUS UNDER 35 USC §103(a) IN VIEW OF IIZUKA *ET AL.* (1994) AND SCOTT *ET AL.* (1979)

The Examiner alleges that claims 5 – 7 are obvious under 35 USC §103(a) in view of Iizuka *et al.* (1994) and Scott *et al.* (1979). The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time of the invention to have used the *Drosophila* cell lysates and *Drosophila* embryo cell lysates of Scott *et al.* in the method of Iizuka *et al.*, and that the motivation to do so is provided by Scott *et al.*

Applicant respectfully disagrees with the Examiner's allegations of obviousness for the following reasons. Applicants have demonstrated above that Iizuka *et al.* do not show a method of protein production using animal cell lysates, where the RNA template includes both a 3' cap and a 5' poly(A) tail and the protein production is greater than the sum of the protein production where the RNA template includes only a 3' cap and the protein production where the RNA template includes only a 5' poly(A) tail.

Iizuka *et al.* and Scott *et al.* either alone or in combination do not teach, suggest, or motivate one skilled in the art at the time the invention was made to provide a method of protein production using animal cell lysates, where the RNA template includes both a 3' cap and a 5' poly(A) tail and the protein production is greater than the sum of the protein production where the RNA template includes only a 3' cap and the protein production where the RNA template includes only a 5' poly(A) tail. In particular, as discussed in the immediate preceding section, Iizuka *et al.* does not teach a method of protein production using animal cell lysates, where the RNA template includes both a 3' cap and a 5' poly(A) tail and the protein production is greater than the sum of the protein production where the RNA template includes only a 3' cap and the protein production where the RNA template includes only a 5' poly(A) tail. Scott et al. does not make up for these deficiencies of Iizuka *et al.*

Thus, a prima facie case of obviousness has not been made and Applicant's respectfully request this rejection be withdrawn. However, to expedite allowance of the application, Applicants submit this amendment to clarify the claimed invention.

Applicants respectfully submit that the claims are ready for examination and in condition for allowance.

Respectfully submitted,

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In the event this paper is deemed not timely filed the applicants hereby petition for an appropriate extension of time. The fee for this extension may be charged to Deposit Account No. 501321 along with any other additional fees which may be required with respect to this paper; any overpayment should be credited to the account. If any fees charged to this Deposit Account will exceed $500, applicant respectfully requests that its counsel be notified of such amounts before the Deposit Account is charged.